Environment International 110 (2018) 123–130

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Mortality burden of diurnal temperature range and its temporal changes: A multi-country study

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ARTICLE INFO

Keywords:
Diurnal temperature range
Attributable mortality risk fraction
Time-varying effect
Climate change

ABSTRACT

Although diurnal temperature range (DTR) is a key index of climate change, few studies have reported the health burden of DTR and its temporal changes at a multi-country scale. Therefore, we assessed the attributable risk fraction of DTR on mortality and its temporal variations in a multi-country data set. We collected time-series data covering mortality and weather variables from 308 cities in 10 countries from 1972 to 2013. The temporal change in DTR-related mortality was estimated for each city with a time-varying distributed lag model. Estimates for each city were pooled using a multivariate meta-analysis. The results showed that the attributable fraction of total mortality to DTR was 2.5% (95% eCI: 2.3–2.7%) over the entire study period. In all countries, the attributable fraction increased from 2.4% (2.1–2.7%) to 2.7% (2.4–2.9%) between the first and last study years. This study found that DTR has significantly contributed to mortality in all the countries studied, and this attributable fraction has significantly increased over time in the USA, the UK, Spain, and South Korea. Therefore, because the health burden of DTR is not likely to reduce in the near future, countermeasures are needed to alleviate its impact on human health.

1. Introduction

Diurnal temperature range (DTR, i.e., the intra-day temperature change) is a well-known weather-related risk factor for human health. Numerous studies have described a positive association between DTR and mortality (Cao et al., 2009; Lim et al., 2015; Tam et al., 2009;

Abbreviations: ARF, attributable risk fraction; DLNM, distributed lag non-linear model

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http://dx.doi.org/10.1016/j.envint.2017.10.018
Received 30 July 2017; Received in revised form 22 October 2017; Accepted 22 October 2017
Available online 28 October 2017

Vutcovici et al., 2014; Yang et al., 2013) and have reported that people who are elderly, less educated, female, or have cardiovascular or respiratory disease are more susceptible to DTR than others (Kan et al., 2007; Lim et al., 2012a; Yang et al., 2013). In addition, because DTR has been reported as an important meteorological indicator closely related to global climate change (Braganza et al., 2004; Kan et al., 2007; Yang et al., 2013), an in-depth investigation of the DTR-mortality relationship is important to comprehensively assess the future health impact of climate change.

Biological mechanisms through which a sudden change in absolute temperature might affect mortality have been described in previous medical and epidemiological studies (Garrett et al., 2009; Garrett et al., 2011; Greenberg et al., 1983; Keatinge et al., 1984; Martinez-Nicolas et al., 2015; Qiu et al., 2013). Sudden changes in within-day temperatures may cause physiological health problems (Garrett et al., 2009; Garrett et al., 2011); unstable weather or temperature changes can lead to the onset of cardiovascular events brought on by increased workload. This can affect the respiratory system by triggering inflammatory nasal responses (Ballester et al., 1997; Carder et al., 2005; Graudenz et al., 2006; Hashimoto et al., 2004; Imai et al., 1999; Luurila, 1980). These mechanisms have been suggested as potential causes of increasing human mortality (Buguet, 2007; Guo et al., 2016).

Based on this biological evidence, previous studies have tried to estimate the risk of DTR on mortality (Lim et al., 2015; Tam et al., 2009; Vutcovici et al., 2014). However, most previous studies assessed the risk of DTR using only relative risk (RR), not the attributable risk fraction, which can quantify the mortality burden. Furthermore, because a majority of the previous studies were conducted in single cities or single countries and used different statistical methods (Kan et al., 2007; Lim et al., 2012a; Yang et al., 2013), results of these studies might have limited applicability on a multi-country scale.

Most previous studies estimated the risk of DTR on mortality using historical data (Kan et al., 2007; Lim et al., 2012a), and the estimated impact of DTR was assumed to be consistent over time. However, this assumption might not be suitable for predicting the health impact of climate change because several factors, including intrinsic biological (e.g., disease/nutrition status) and extrinsic factors (e.g., forecast and infrastructure improvements, local environment, or social system conditions), can modify the population's vulnerability to absolute temperature and rapid temperature change within a day (Gasparrini et al., 2015a; Linares et al., 2014; Wu et al., 2014). Therefore, it is important to assess temporal change in the DTR-related mortality relationship to examine whether people are adapted or mal-adapted to DTR.

In this study, we assessed the percent increases in risks and the attributable risk fraction of DTR for 308 cities of 10 countries. We examined whether the excessive risks and attributable risk fractions changed during the study period. We used a Multi-Country Multi-City (MCC) Collaborative Network to assess the impact of weather on mortality using a multi-country data set referenced in previous papers (Gasparrini et al., 2015a; Gasparrini et al., 2016; Guo et al., 2014; Guo et al., 2016).

2. Material and methods

2.1. Data

Time-series data covering mortality and weather variables were collected from 385 locations in 10 countries: Canada (26 cities, 1986–2011), the United States (USA) (135 cities, 1985–2006), Brazil (18 cities, 1997–2011), Colombia (5 cities, 1998–2013), the United Kingdom (UK) (10 regions, 1990–2012), Ireland (6 regions, 1984–2007), Spain (51 cities, 1990–2010), Japan (47 prefectures, 1972–2012), South Korea (7 cities, 1992–2010), and Australia (3 cities, 1988–2009). For convenience of interpretation, the location is described as “city” in this study. The daily mortality count is the daily count of death for all causes. If a daily count of all causes of death was not available for a city, then death for non-external causes (ICD-9: 0–799, ICD-10: A00-R99) was used instead. The DTR was chosen as the exposure index, computed from monitoring stations as the difference between the daily maximum and daily minimum temperatures. Detailed information regarding data collection is provided in the Supplementary material (data details).

2.2. First-stage time series model

The first-stage time series model was divided into a two-step procedure. First, a time-series regression was applied, based on a generalized linear model using a quasi-Poisson distribution with parameters for DTR, the day of week, the seasonal long-term trend, the inter-day temperature change (the change in mean temperature between two neighboring days), and absolute temperature. We modeled the DTR-response curve with a linear function and the lag-response curve with two internal knots placed at equally spaced values on a log scale using a natural cubic B-spline with 14 days of lag. The inter-day temperature change was adjusted in the same way as DTR. We also modeled the temperature-response relationship using a quadratic B-spline with three internal knots (placed at the 10th, 75th, and 90th percentiles of location-specific temperature distributions) and a lag-response (up to 21 days) curve with natural cubic B-spline with three internal knots placed at equally spaced values on the log scale. This modeling approach was used in a previous multi-country temperature-mortality study using a distributed lag non-linear model (DLNM) (Gasparrini et al., 2010; Gasparrini et al., 2015b). Seasonal trends were adjusted using a natural cubic B-spline of time with eight degrees of freedom (df) per year (df = 8), and the day of week was included as an indicator variable. Results of the first stage estimated the association between DTR and mortality for each city.

2.3. Time varying distributed lag non-liner model

The DLNMs, described in the first-stage analysis, assumed that the exposure-lag-response associations between DTR and mortality in each location were constant across the whole study period. We also applied a time-varying DLNM with a linear interaction (Gasparrini et al., 2015a; Gasparrini et al., 2016) between DTR and year. Using the time-varying DLNM, we derived coefficients representing the exposure-lag-response association for the first and last year of the study period for each city. The set of four coefficients (the entire period, the first year, and the last year for each location) were reduced to one coefficient that modeled the overall cumulative associations between DTR and mortality. The sets of four coefficients were used to determine the lag-response relationships at the 99th percentile of the DTR reference at 0 °C DTR.

2.4. Second stage meta-analysis

We pooled one parameter of the overall cumulative exposure-response relationship and the four parameters of the lag-response relation. Multivariate random-effect meta-regression was used to pool the parameters by country. We used indicators of country as predictors in the meta-regression to country-pooled estimates and city-specific predicted parameters (Best Linear Unbiased Prediction, BLUP). The overall pooled coefficient (only for calculating excessive relative risk for all countries together) was estimated by meta-analysis without predictors. All analyses were performed using R software (version 3.3.1) packages dlnm and mvmeta (Gasparrini, 2011; Gasparrini et al., 2012; Gasparrini et al., 2010).

2.5. Attributable mortality risk faction

Overall cumulative relative risk estimated from BLUP for each city was used to compute the attributed number of deaths and the fraction of deaths over the following 14 days at each location. The total number

Table 1
Descriptive statistics by country. Including distribution of diurnal temperature range in first 3 years (First) and last 3 years (Last) of country-specific study periods.

Country (# of city)	Time period	Total deaths	Study period (year)	Absolute temperature (°C)	Diurnal temperature range (°C)					
				Mean	Mean	10%	25%	50%	75%	90%
Canada	Whole	2,989,901	1986–2011	6.8	10	4.4	6.6	9.7	13	15.9
(26)	First			7	10.1	4.5	6.7	9.8	13	16
	Last			6.9	9.9	4.4	6.4	9.4	12.9	16.1
USA	Whole	22,896,409	1985–2006	14.8	10.9	5.6	7.8	10.6	13.9	16.7
(135)	First			14.7	11	5.6	7.8	10.6	13.9	17.2
	Last			15.1	10.7	5.6	7.8	10.6	13.3	16.1
Brazil	Whole	3,435,502	1997–2011	24.2	9	5.4	6.8	8.6	10.7	13.2
(18)	First			24.1	8.8	5.1	6.6	8.4	10.6	13.1
	Last			24.3	9.1	5.5	7	8.6	10.7	13.4
Colombia	Whole	956,539	1998–2013	23.4	9	5.8	7	8.8	10.8	12.4
(5)	First			23.1	8.9	5.6	6.8	8.7	10.8	12.5
	Last			23.5	8.9	6.1	7.2	8.7	10.4	12.1
UK	Whole	1,2075,786	1990–2012	10.3	7.3	3.8	5.2	6.9	9.1	11.3
(10)	First			10.1	7.3	3.8	5.1	6.9	9.1	11.3
	Last			10.1	7.5	3.9	5.3	7	9.4	11.7
Ireland	Whole	1,058,215	1984–2007	9.7	6.7	3.4	4.8	6.4	8.3	10.3
(6)	First			8.9	6.8	3.6	4.9	6.5	8.4	10.4
	Last			10.3	6.9	3.6	4.9	6.6	8.5	10.5
Spain	Whole	3,480,531	1990–2010	15.5	10.6	4.9	7	10	13.8	17
(51)	First			15.1	10.7	5	7.2	10.2	13.8	17.2
	Last			15.5	10.4	4.8	6.8	9.8	13.6	17
Japan	Whole	3,6113,897	1972–2012	15.1	8.4	4.2	6	8.2	10.6	12.8
(47)	First			14.4	8.8	4.4	6.3	8.6	11	13.3
	Last			15.5	8.2	4.1	5.9	8	10.2	12.4
South Korea	Whole	1,727,642	1992–2010	13.7	8.2	4.1	5.9	8	10.2	12.7
(7)	First			13.5	8	3.8	5.6	7.7	10.1	12.5
	Last			13.8	8.3	4.3	5.9	8	10.3	12.7
Australia	Whole	1,177,950	1988–2009	18.1	8.2	4.4	5.9	7.8	10	12.4
(3)	First			18.1	7.8	4.1	5.6	7.3	9.5	11.9
	Last			18.7	8.1	4.5	5.8	7.6	10	12.6

USA: United States of America, UK: United Kingdom.

of deaths attributed to DTR was calculated as the sum of all days in the series when DTR contributed to death and its ratio with the total number of deaths; this provides the 'total attributable fraction' (Gasparrini and Leone, 2014). We also computed the time-varying attributable risk of DTR based on the BLUP for each city from the time-varying DLNM. Although time-dependent distributions of DTR and death could be used to estimate time-varying attributable risk, we used DTR and the mortality distribution for the entire period because we did not find a clear difference between DTR distributions for the first and last three years of the series for each city (Table 1).

2.6. Sensitivity analysis

In order to test the sensitivity of our results to the modeling parameters and assumptions described above, we changed lag days for DTR (21 days), inter-day temperature changes (10 and 21 days), and the df of lag knots for DTR (df = 5), and we analyzed the first results. We also assessed sensitivity to controlling for humidity (only for six countries that had relative humidity data), air pollution (Korea: O_3 and PM10), flexibility of long-term trend (df = 7 and 9), and absolute temperature using various knot percentiles and changing lag days (14 and 28 days).

3. Results

Descriptive statistics of mortality, absolute temperature, and the distribution of DTR are in Table 1. Fig. 1 displays the geographical distributions of the 308 cities within the 10 countries included in the analyses and the corresponding annual averaged DTR (°C). The data set included 85,912,372 deaths. Variability in DTR was observed among countries over the entire study period, with mean values ranging from 6.7 °C (Ireland, six cities) to 10.9 °C (USA, 135 cities). Table 1 also lists the DTRs and absolute temperature distributions during the first and second halves of the study period for each country. As expected, the mean temperature increased slightly over time, although we did not detect a clear temporal pattern in the DTR values. City-specific descriptive statistics are reported in Supplementary Table S1.

The percent increases in risks and attributable mortality risk fractions of DTR estimated from the model with no interaction (i.e., the average throughout the study period) are reported in Table 2. Percent increases in risks of DTR (per 10 °C) were highest in South Korea (6%, 95% CI: 3–9.1%), Spain (4.4%, 3–5.8%), and Brazil (4.2%, 1.7–6.7%). Colombia (−1.2%, −6.3–4.1%) and Ireland (0.3%, −3–3.8%) showed the lowest percent increases in risk of DTR, although both were not significant. Table 2 also displays the total percentage of deaths attributable to DTR (reference at minimum DTR of each city, 2.5% with 95% empirical confidence interval (95% eCI): 2.3–2.7%). Similar with percent increases in risk, most of the country-specific estimated attributable risks were statistically significant. The risk fraction was highest in Korea (4.5%, 3–5.9%) and Spain (4.2%, 3.5–4.9%). The fractions were lowest in Colombia (−1.5%, −5.1–2.1%) and Ireland (0.2%, −1.2–1.4%).

Fig. 2 displays the country-pooled lag-response associations at the 99th percentile of DTR referenced at 0 °C. The coldest (Canada, Ireland, and UK) and warmest (Brazil and Colombia) countries showed the highest RR at lag 0 and lasted to a lag of 4–7 days. Other countries, which had moderate temperatures, had the highest RR in approximately 1–3 lag days and were limited to a lag of 7–14 days. The corresponding city-specific lag-response is displayed in Supplementary Fig. S1.

Results from an analysis of the temporal variation in the percent increases in risk of DTR are illustrated in Fig. 3. Table 3 displays the temporal variation of estimates per year and test results for linear interaction (null hypothesis is the pooled interaction term is zero; the null hypothesis is that no temporal change occurred). The percent increase

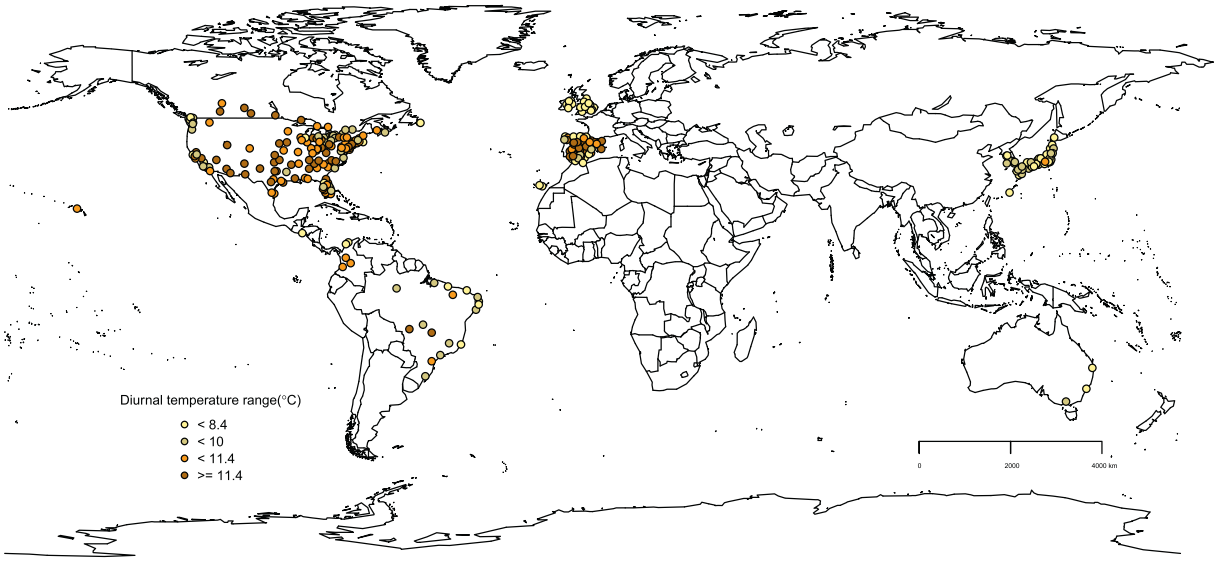

Fig. 1. Geographical locations of study cities and their annual mean values of diurnal temperature range (DTR, °C).

Table 2
Percent increases in risk (per 10°C) and attributable risk fraction (%) of diurnal temperature range on mortality by country.

Country	Percent increases in risk (%, 95% CI)	Attributable risk fraction (%, 95% eCI)
Canada	2.6% (0.9, 4.2)	2.7% (1.8, 3.5)
USA	2.9% (2.3, 3.6)	3.2% (2.9, 3.5)
Brazil	4.2% (1.7, 6.7)	3.7% (2.6, 4.9)
Colombia	− 1.2% (− 6.3, 4.1)	− 1.5% (− 5.1, 2.1)
UK	2.9% (1.5, 4.4)	2.1% (1.6, 2.7)
Ireland	0.3% (− 3, 3.8)	0.2% (− 1.2, 1.4)
Spain	4.4% (3, 5.8)	4.2% (3.5, 4.9)
Japan	3.1% (2.3, 3.9)	2.7% (2.4, 3)
South Korea	6% (3, 9.1)	4.5% (3, 5.9)
Australia	4.2% (0.7, 7.9)	3.3% (1.1, 5.3)
Overall	3.1% (2.7, 3.5)	2.5% (2.3, 2.7)

USA: United States of America, UK: United Kingdom, eCI: empirical confidence interval.

in risk of DTR increased from 2.5% (95% CI: 1.8–3.3%) to 3.8% (95% CI: 3.1–4.5%) between the first and last periods. Except for Ireland and Japan, all countries showed patterns of increasing percent increases in DTR risk, with − 2.9–5% in the first year and 1.5–13.8% in the last year of the data. The temporal increase of percent increases in DTR risk were significant (P-value < 0.05) for the USA, the UK, Spain, and South Korea (Table 3). Country-pooled temporal changes in the lag-response relationship are displayed in Supplementary Fig. S2. A comparison between the curves suggested that a longer lag-association and smaller harvesting effect were present in most countries.

Fig. 4 and Table 3 display the temporal variation in the attributable mortality risk fraction of DTR. Overall, the attributable risk fraction of DTR to deaths increased from 2.4% (95% eCI: 2.1–2.7%) to 2.7% (2.4–2.9%) between the first and last periods. The increase in the attributable risk fraction of death overtime was observed in all countries except Japan (0.07% decrease per year) and Ireland (0.23% decrease per year). Korea (0.56% per year) and Colombia (0.31% per year) showed the fastest increase in the risk fraction of death, whereas Canada (0.03% per year), the USA (0.09% per year,) and the UK (0.11% per year) showed the slowest increase over time. Corresponding city-specific estimates are reported in the Supplementary material (Supplementary Table S2). The main conclusions were found to be robust based on the sensitivity analysis (Supplementary Table S3).

4. Discussion

Our findings showed that DTR is responsible for an increasing mortality risk (3.1%, 95% CI: 2.7–3.5%) and fraction of deaths (2.5%, 95% eCI: 2.3–2.7%) in all the countries studied. South Korea and Spain showed the highest percent increase in risk (6% and 4.4%, respectively) and attributable risk fractions (4.5% and 4.2%, respectively). This study also provides evidence of the incremental health impact of DTR during the last few decades. Except for Japan and Ireland, an increasing pattern of percentile increases in risks (3.8% in the last year of the study periods, compared with 2.5% in the first year) was observed, and the attributable risk fraction showed the same temporal pattern (2.7% in the last year of the study period, compared with 2.4% in the first year).

This study is comparable to a recent temperature variability-mortality association study in the MCC Collaborative Network (Guo et al., 2016). Both studies were based on a similar multi-country data set and addressed the significant association between temperature variability and mortality, even after controlling for the main effect of absolute temperature. Guo et al. developed a new composite index of intra- and inter-day temperature variability using a standard deviation of minimum and maximum temperatures during the exposure days, and found the temperature variability-mortality relationship varied with exposure days (0–7 days), countries (twelve countries/regions with 372 communities), and season (cold, hot, and moderate). Meanwhile, our study focused on the association between intra-day temperature variability and mortality, using a classical meteorology index (DTR) and flexible statistical method, which considered a flexible lag-response structure of DTR. In addition, our study included data from 308 cities in 10 countries with > 15 years of study data to estimate the temporal changes in the DTR-mortality association. We also found an overall increase in the health burden of DTR on mortality during recent decades.

Our finding suggested that the DTR effects on mortality were higher in warmer countries (Brazil, Australia, and Spain) compared to colder countries (Canada, Ireland, and the UK), although Korea and Colombia were exceptions. These findings are consistent with previous studies, such as multi-country studies that reported that the effect of temperature variability with short exposure durations (0–1 and 0–2 days) on mortality is higher in hot area (> 22.9 °C) than other areas (cold, moderately cold, and moderately hot areas) (Guo et al., 2016). Studies from the USA also showed a higher DTR effect in southern areas (percent change of non-accidental mortality per one unit of DTR 0.24–0.31%) than other regions (0.22–0.27%) (Lim et al., 2014).

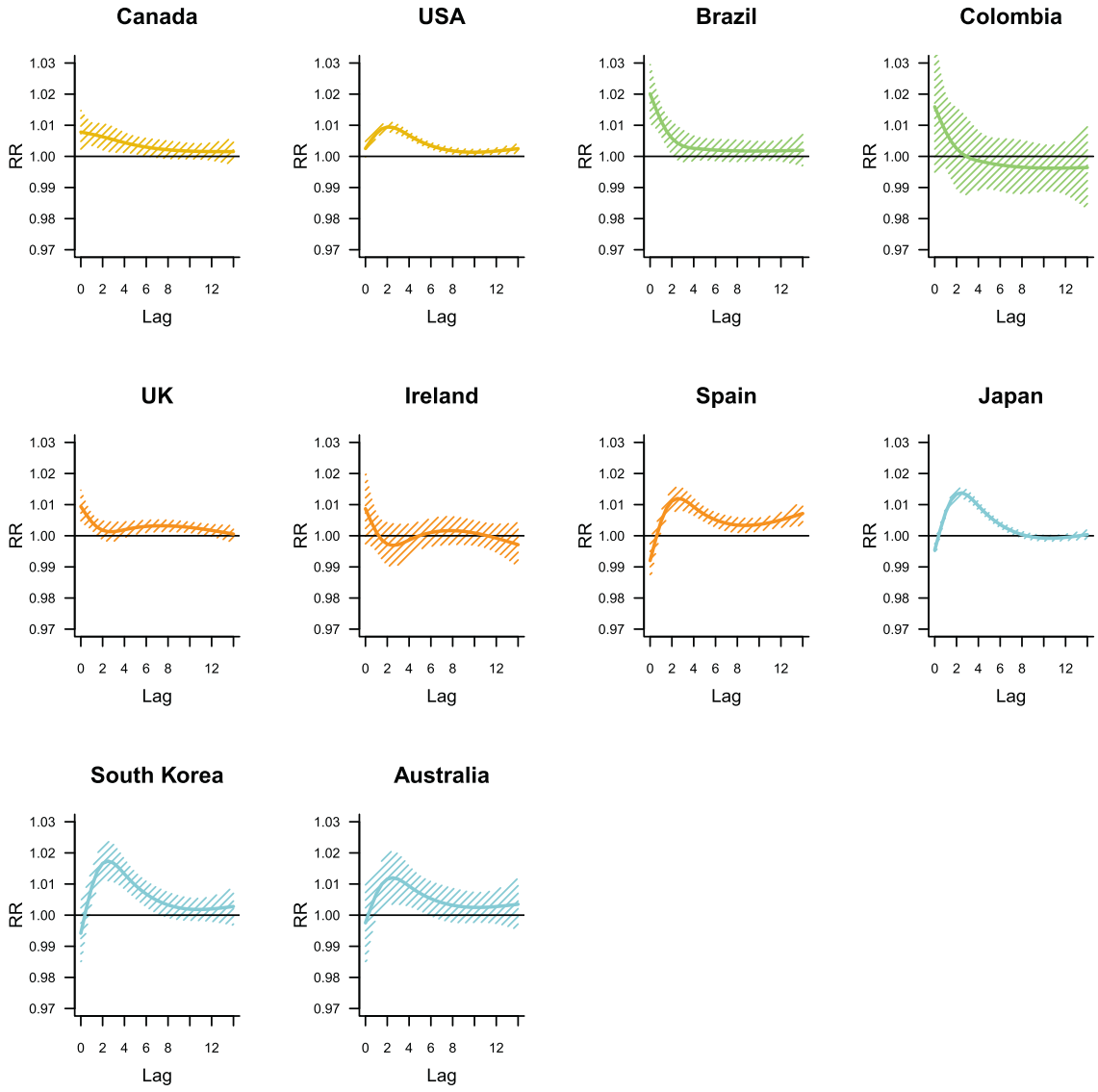

Fig. 2. Lag-response relationship between diurnal temperature range (DTR) and mortality predicted for the overall study periods of 10 countries; RR: relative risk. USA: United States, UK: United Kingdom.

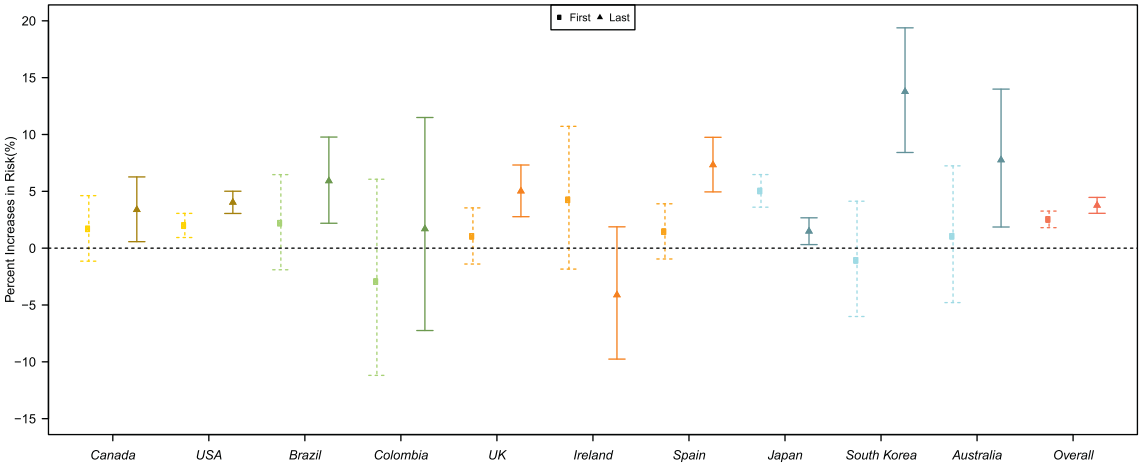

Fig. 3. Temporal changes in percent increases in risk (%) between the first (First) and the last (Last) year of country-specific study periods; USA: United States, UK: United Kingdom.

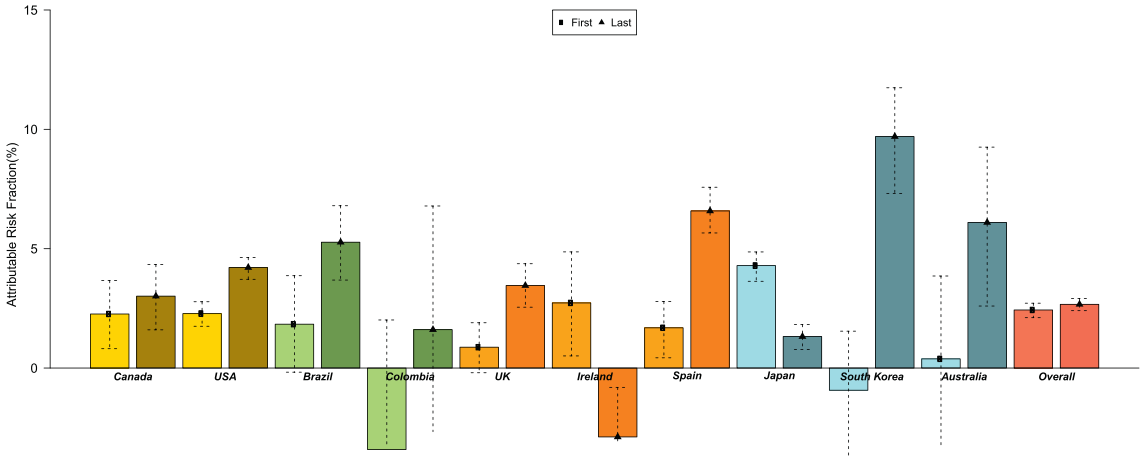

Fig. 4. Temporal changes in attributable risk fraction (%) between the first (First) and the last (Last) year of country-specific study periods; USA: United States, UK: United Kingdom.

Table 3
Variation of excessive relative risk (per 10°C) and attributable fraction (%) of diurnal temperature range on mortality per a year, and P-value of the test.

Country	Study period (years)	Variation (per year)		P-value[a]
		Percent increases in risk	Attributable risk fraction	
Canada	26	0.06%	0.03%	0.4384
USA	22	0.09%	0.09%	0.0209
Brazil	15	0.25%	0.23%	0.2243
Colombia	16	0.29%	0.31%	0.6583
UK	23	0.17%	0.11%	0.0344
Ireland	24	− 0.35%	− 0.23%	0.0989
Spain	21	0.28%	0.23%	0.0025
Japan	41	− 0.09%	− 0.07%	< 0.0001
South Korea	19	0.78%	0.56%	< 0.0001
Australia	22	0.3%	0.26%	0.1543

USA: United States of America, UK: United Kingdom.

[a] Significant test on temporal change by Wald type test of the pooled reduced coefficient of the year-interaction terms. The null hypothesis is that no change in year occurred.

Studies in China also showed a similar trend of a relatively higher and more significant effect of DTR in warmer cities (Guangzhou and Shanghai) than colder cities (Anshan and Xi'an, although Tangshan is an exception).

To specifically assess the association between the DTR effects and the annual mean of absolute temperature, we fitted a weighted regression model (Supplementary Fig. S3) to our data; a city-specific BLUP of the DTR coefficient (i.e., log of relative risk estimated from the second stage analysis) was used as a response variable, annual mean temperature was used as an explanatory variable, and inversed city-specific variances of the DTR coefficient were used as weights. We observed a significantly positive linear association between the DTR effect and the annual mean temperature from the weighted regression model (P-value = 0.01). This result can be interpreted as evidence to support the hypothesis that there may be an impact on mortality from the positive interactions between long-term temperature and DTR.

The synergism effect of the DTR and long-term temperature on mortality may be due to many factors. One mechanism may be aggravation. Hot temperatures can disturb normal physiological thermoregulation, including changes in blood viscosity, plasma cholesterol levels, and the red blood cell count (Keatinge et al., 1986). Increasing DTR may also impact mortality by lowering the thermoregulatory system and negatively affecting the heart rate, heart rate variability, blood platelets, red blood cells, and blood viscosity (Keatinge et al., 1984; Lim et al., 2012b). Because warm countries are exposed to hot weather more often, the DTR effect in warm areas can be amplified by the increase in the biological burden. Another hypothesis is that the effect of the DTR is higher in warm areas because people in warm and moderately warm areas are more likely to keep their windows open and spend more time outdoors, which may increase exposure to DTR, thus increasing the effects of DTR. However, our results only suggested the aggravation hypothesis; further research should be conducted to find the causal relationship between DTR and annual mean temperature on mortality.

Our research found that the effect of DTR on mortality changed across time. We speculate several plausible explanations. The first hypothesis is deterioration by climate change, suggested in the previous paragraph. We found higher risk and greater risk increases in hot cities. This finding suggests that climate change may increase the risk of DTR. Secondly, an aging population may also be a crucial factor, as numerous studies have revealed that elderly people are more susceptible to DTR (Kan et al., 2007; Lim et al., 2012a; Yang et al., 2013), and the populations of developed and developing countries included in our research are aging (Börsch-Supan, 2008; Faunce, 2008).

In the results (Table 3), we found that the increasing rate of the DTR effect on mortality was higher in warmer countries (percent increase in risk per year was 0.25–0.3% for Brazil, Colombia, Spain, and Australia) compared to other countries (− 0.35–0.17%)(except for Korea (0.78%)). These results suggested that there may be an association between long-term temperature and the increasing mortality rate for the DTR effect. Our study did not consider this relationship because of data limitations and the disparity in study periods. As well, some confounding factors need to be considered to understand this association between temperature and the DTR effect. If there is a positive correlation between warming and the effect of DTR, then the degree of climate warming by country should be considered as a confounding variable. The rate and extent of aging in each country should also be investigated. Furthermore, each country has disparate weather forecasting systems, accessibility to medical care, public health services, national income, and social infrastructure, all of which can affect the mortality burden of DTR. Therefore, these variables should be considered comprehensively, and additional research on this topic is needed.

Although not found in our study, prior studies have reported that climate change factors (greenhouse gases, urbanization, and aerosols) have led to a global decline in the DTR during the twentieth century because the nocturnal minimum temperatures have increased faster than the maximum temperatures (Braganza et al., 2004; Makowski et al., 2008). In addition, Brown et al. (2017) found that the variability of low-frequency global mean surface air temperature (GMST) will likely decrease under climate warming. They suggested that the reduction in high-latitude surface albedo variability by a climatological

reduction in albedo was a major reason for this reduction in GMST variability (Brown et al., 2017). However, it is still unclear how this decline in the DTR will affect human health, and how the extend and intensity of the DTR variation will change depending on the climate and geographical conditions. Previous studies reported that the DTR values in some regions have not declined during past decades despite the global reduction (Easterling et al., 1997). Brown et al. (2017) found that local surface air temperature variability in tropical and subtropical land areas can increase with climate change (Brown et al., 2017). Also, given that increasing nocturnal temperatures can affect mortality and the distribution of DTR simultaneously, a confounding effect of the nocturnal temperatures needs to be considered to estimate the effect of DTR on death. Even if the effect of increasing nocturnal minimum temperature is partly considered in our study by controlling the daily averaged temperature, there is a limitation to controlling the effect of nocturnal temperature due to lack of data. Therefore, future research should be conducted using various climate conditions with longer study periods and more detailed weather data.

As described earlier, although DTR and absolute temperature may affect human health in diverse ways, because both have a mechanism that negatively affects human health, the effect of absolute temperature and temperature variability on mortality has been an interesting topic of environmental research. In addition, comparing the health effects of two variables has important implications for understanding human health in a climate change context (which can increase both the average values and the variability of temperature)(Guo et al., 2016; Stocker, 2014; Vicedo-Cabrera et al., 2016). Recent studies asserted that DTR has a lesser effect than absolute temperature on mortality (Lee et al., 2017; Vicedo-Cabrera et al., 2016). Our results also suggest a lesser effect of DTR on mortality when compared with the total attributable mortality fraction of absolute temperature from a previous study (Gasparrini et al., 2015b). The total fraction of DTR attributed to mortality (2.5%) was much smaller than the fraction for total absolute temperature (7.71%) (Gasparrini et al., 2015b). However, our results may differ from the conclusions of previous studies (Chen et al., 2007; Kan et al., 2007; Lim et al., 2015; Tam et al., 2009; Yang et al., 2013) that used modeling strategies that did not fully control the flexible lag structure of absolute temperature. The estimates of DTR on mortality could be overestimated unless the main effects of temperature are fully adjusted because the effect of absolute temperature is delayed up to several weeks after exposure. Hence, we contend that our modeling approach provides more appropriate results for estimating the health effects of DTR when compared with previous studies.

In this study, more acute DTR-mortality relationships (highest RR at 0 lag days) were observed in warmer and colder countries (Brazil, Colombia, Canada, Ireland, and the UK). In contrast, delayed DTR-mortality relationships (highest RR at 2–4 lag days) were observed in moderate temperature countries. Although this study did not study this difference, we speculate that the specific factors are related to physiological, technological, and behavioral adaptations to the climate.

A key strength of our study is the use of a large multi-country, multi-city data set with different demographic distributions, climate conditions, and socio-economic characteristics. To the best of our knowledge, our study is the largest of its kind including 308 locations and > 85 million deaths from 10 countries. Our study also is the first and the largest study of time-varying DTR-related mortality, and the use of a uniform statistical framework across all cities makes the results directly comparable. In addition, unlike previous studies that have quantified the association using RR (Kan et al., 2007; Vicedo-Cabrera et al., 2016; Yang et al., 2013), our study used the attributable mortality burden of DTR. Because the attributable fraction considers the distribution and risks of each variable, the attributable fraction is a suitable measure to estimate the mortality burden of the exposure variable and to establish corresponding public health strategies.

However, our study had some limitations that must be acknowledged. First, our findings are not globally representative because regions of Africa and large countries in Europe and Asia (such as France, Russia, and India) were not included in this study. Second, the data did not include age- or gender-specific mortality rates, which could be explored in future research. We could only identify the association between DTR and all-causes of mortality and not the causal effect of DTR on mortality. Future studies should strive to overcome these limitations by expanding the study population and modifying the study design.

5. Conclusions

In summary, this study found that there was a significant effect of DTR on mortality across all countries, and provided evidence that the effect of DTR was higher in warmer regions. Although our estimated attributable mortality fraction of DTR was smaller than risk fractions of absolute temperature from a previous multi-country study (Gasparrini et al., 2015b), it was higher than risk fractions of extreme heat and cold temperatures. In addition, although the risks and contributions of DTR to mortality varied for each country, it increased at the multi-country scale with significant increases estimated for the USA, the UK, Spain, and South Korea; we found non-significant increments for Canada, Brazil, Colombia, and Australia. The estimates of DTR-related mortality increased throughout the study period in all countries, which could be interpreted as maladaptation to DTR. This indicates that the health burden of DTR is not likely to decrease in the near future. Hence, we suggest that public-health policies and climate change research that have so far focused on the effects of extreme heat should be extended to account for the health burden of DTR and its temporal variations.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2017.10.018.

Acknowledgements

This study was supported by the Global Research Lab (#K21004000001-10A0500-00710) through the National Research Foundation of Korea.

Competing financial interest

The authors declare they have no actual or potential competing financial interests.

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